PATENT COOPERATION TREATY

| From the INTERNATIONAL SEARCHING AUTHORITY | PCT | | |
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| To: ISENBRUCK BÖSL HÖRSCHLER WICHMANN HUHN Attn. Wichmann, Hisenbruck Bösl Hörschler Prinzregentenstrasse Postfach 860880 D-81675 München GERMANY 30, Nov. 2004 | NOTIFICATION REGARDING REVIE OF JUSTIFICATION FOR INVITATION TO ADDITIONAL SEARCH FEES (PCT Rule 40.2(e)) | PAY | |
| FEES Frist: 26 - 12 . 04 Vorfrist: 16 12 . 04 | Date of mailing (day/month/year) 26/11/2004 | B1 HJW | |
| Applicant's or agent's file Wistrence C62780PC | PAYMENT DUE ONLY if item 1 applies: within ONE MONTH from the above date of mailing | B3 | |
| International application No. PCT/EP2004/005208 Applicant | International filing date (day/month/year) 14/05/2004 | Sekr HG | |
| CYTOS BIOTECHNOLOGY AG | | Ablg. | |
| The applicant is hereby notified that, with regard to the protest filed on this International Searching Authority has reviewed the justification for the invitation to pay additional search fees (Form PCT/ISA/206) and the applicant is invited to pay a protest fee, within the time limit indicated above, for further examination of the protest, in the amount of (currency/amount) or, _EUR_1_020_00 because x the invitation is justified. the invitation is justified in part. To the extent the invitation is not justified, additional search fee(s) paid under protest will be refunded in due course. The reasons for this invitation to pay a protest fee are indicated in the Annex. Failure to pay the protest fee within the time limit indicated above will result in the protest being considered withdrawn. | | | |
| The applicant is hereby notified that, with regard to the protest filed on this International Searching Authority has reviewed the justification for the invitation to pay additional search fees (Form PCT/ISA/206) and has found that the invitation was not justified. Any additional search fee(s) paid under protest will be refunded in due course. | | | |
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| Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo.nl, Fax: (+31-70) 340-3016 | Anna Rauf | | |

Nach Regel 93 b) EPÜ von der Akteneinsicht ausgeschlossen Pursuant to Rule 93 b) EPC excluded from file inspection Pièce exclue de l'inspection publique en vertu de la règle 93 b) CBE

| Application | number: |
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| Application | |

EP2004/005208

Internal Notes

Result of the Prior Review according to Rule 40.2(e) PCT for EP0405208

The objection under lack of unity raised in the ISR is maintained for the following reasons:

The requirements of unity of invention (Rule 13 PCT) are not fulfilled in that there is no technical relationship among the inventions as they do not involve one or more of the same or corresponding special technical features.

Claim 1 refers to a method for selecting at least one antigen-specific B cell from a mixture of cells comprising: a mixture of cells comprising B cells, a first composition comprising a core particle, at least one antigen, wherein the antigen and the core particle form through association an ordered and repetitive antigen array, contacting the first composition with said mixture of cells, labelling the composition and the B cells independently and selecting a B cell which is positive for said first and second labelling compound. Claim 2, refers to the different core particles used: a virus, a virus-like particle, a bacteriophage, a bacterial pilus, a viral capsid particle and a virus-like particle of a RNA-phage. According to Rule 13 PCT a group of inventions is considered to be unitary only if so linked as to form a single general inventive concept. The sole concept linking independent claim 1 and the different core particles of claim 2 is the use of said core particles for the isolation of antigen-specific B-cells by forming an ordered and repetitive antigen array. However, the use of virus-like particles for the isolation of antigen-specific B-cells is already known in the art.

Thus, in the light of the prior art, the problem to be solved by the present application can be formulated as follows: How to isolate further antigen-specific B-cells by core particles forming an ordered and repetitive antigen array. The solution to this problem is a composition comprising a core particle and an antigen according to present claim 1. However, the use of a Rotavirus derived virus-like particle for the isolation of Rotavirus-specific B-cells is known from the prior art (see J. Immunol. Methods (D1), vol.

Rotavirus-specific B-cells is known from the prior art (see J. Immunol. Methods (D1), vol. 275, 2003, pg.: 223-237, abstract, page 224, col. 2, second para. to page 225, col. 1, para. 1, figure 1; page 235, col. 1, third para. to page 236, col. 1, second para.). Moreover, the Review Board is of the opinion that D1 is also detrimental to the concept of an ordered antigenic composition array as referred to in claim 1 for the following reasons:

Claim 1 refers broadly to a composition comprising a "core particle" and an antigen. D1 discloses on page 224, second col., second paragraph that the RV virus-like particle consists of recombinantly produced proteins VP2, VP6 and VP7 wherein VP6 and VP7 are

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strongly antigenic in contrast to VP2. VP2 must therefore be covered by the two other antigenic proteins meaning that it acts as a "core or nucleation particle" for the two other antigens. The Review Board would like to point out that neither the term "core particle" nor the term "antigen" is defined in claim 1 and have therefore to be broadly interpreted. Thus, the RV VLPs of D1 are at the same time "core particles" according to claim 2 as well as a composition according to claim 1 forming a highly repetitive antigenic structure comprising a core particle and an antigen. Additionally, the application itself uses a Hepatitis B core antigen being a single protein as a "core particle" (see example 1 of the present application). All the other method steps of claim 1 are disclosed in D1 starting from page 225 fig. 1 and col. 2, second para. to page 226, col. 1, last para.). Thus, D1 is clearly detrimental to the novelty of the concept of present claim 1. Consequently, all the other core particles mentioned in claim 2 constitute separate alternative solutions to the problem mentioned above. Thus, there is no longer a technical relationship between the six core particles mentioned above.

Consequently, the lack of unity objection is upheld and neither refund of the additional search fee can be granted nor the search over the whole ambit as requested by the applicant in his letter of 20.09.2004. An additional search will be carried out for the group 6 invention as requested.

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